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09/744,289	08/01/2001	Shousun Chen Szu	2026-4282US	3981

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EXAMINER
PORTNER, VIRGINIA ALLEN

ART UNIT	PAPER NUMBER
1645	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/744,289	Applicant(s) Szu et al
	Examiner Portner	Art Unit 1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 1, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-41* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-41* is/are rejected.

7) ☒ Claim(s) *8, 9, and 40* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 3
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-41 are pending.

Priority

1. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed on or after November 29, 2000, any claim for priority must be made during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2) and (a)(5). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c).A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) a surcharge under 37 CFR 1.17(t), and (2) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Commissioner may require additional information where there is a question whether the delay was unintentional. The petition should be directed to the Office of Petitions,Box DAC, Assistant Commissioner for Patents, Washington, DC 20231.

Information Disclosure Statement

2. The information disclosure statement filed April 20, 2001 has been considered.

Claim Rejections - 35 U.S.C. § 101

3. 35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 26 is not directed to an isolated and purified antibody and therefore reads on a product of nature; the claimed invention is directed to non-statutory subject matter.

Claim Objections

5. Claims 8-9, 40 are objected to because of the following informalities:

a.Claims 8 and 9 are identical; claim 9 is duplicative of claim 8.

b. Claim 40 recites the term "coprising"; it should be --comprising--. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 13-17,32-33,41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13-17 recite a combination of conditional claim limitations "the composition is capable, upon injection into a human". The claimed invention is directed to a composition, not a method of immunization. The composition does not comprise any specific amount of conjugate, but must only be capable of the recited functional characteristics when the composition is administered to a human. Claims 13-17 are not further limiting of claims 10-12, from which they depend, because the claim limitations set forth are in the future tense.

Claim 32 recites the phrase "vaccinating a mammal" and "administering to the human"; the term "human" lacks antecedent basis in claim 32.

Claim 33 recites the phrase "wherein the mammal is a human and depends from claim 32; claim 32 already defined the mammal to be a human. Claim 33 is not further limiting of claim 32.

8. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: no methods step of administering a composition to a mammal is recited; only an intended use is set forth. No positively recited methods steps are encompassed by instant claim 41. This rejection could be obviated by amending the step to recite "A method" --comprising the step of-- "administering" --the-- "composition of claim 40 to a mammal".

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-3,6,8-9,10-17,19-26,30-34 and 40 are rejected under 35 U.S.C. 102(a) as being anticipated by Konadu et al (February 1998, different inventive entity).

(Instant claims 1, 34) Konadu et al disclose the instantly claimed invention directed to a conjugate molecule comprising the E.coli O157:H7 O-specific polysaccharide covalently bound to B-subunit of Shiga toxin I (see page 386, col. 2, first paragraph).

(Instant claim 10) An additional embodiment disclosed is the E.coli O157:H7 O-specific polysaccharide covalently bound to a carrier protein, in an acceptable carrier and administered in 0.5ml intramuscular injectable compositions (see page 384, col. 1, paragraph 1, lines 15-16).

(Instant claim 11, 12, 34) The carrier protein was either recombinant Pseudomonas

aeruginosa exoprotein A, or the B-subunit of Shiga toxin 1 (see Materials and Methods, page 383, col. 2, paragraph 4 and page 386, col. 2, paragraph 1).

(Instant claim 13-17) The composition comprised 25 ug of O157 polysaccharide (see page 384, col. 1, paragraph 1, bottom of paragraph). The composition was capable of inducing anti-O157 polysaccharide titers that were bacteriocidal (see Table 2, page 385). The human serum IgG, IgM and IgA antibodies were measured at weeks 1, 4 and 26 and activity measured based upon ELISA units, which showed more than a 50% rise for IgG antibodies.

(Instant claims 19-21, 30-33) The disclosed compositions were administered to a mammal, the method comprising the step of : administering to said mammal, in a physiologically acceptable carrier, a conjugate molecule of claim 1. The dosage was about 5 to about 50 micrograms of E.coli O157 O-specific polysaccharide, specifically 25 micrograms (see page 384, col. 1, paragraph 1, line 14 to the end of the paragraph).

(Instant claims 22-26, 40) Compositions of serum antibodies immunoreactive with E.coli O157 O-specific polysaccharide and with the B-subunit of Shiga toxin 1 (see Table 1, 2, and page 386, col. 2, first paragraph). The reference anticipates the instantly claimed invention.

11. Claims 10-17,22, 24, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Konadu et al (November 1994).

(Instant claim 10-12) Konadu et al disclose the instantly claimed invention directed to a conjugate molecule comprising the E.coli O157:H7 O-specific polysaccharide covalently bound to carrier protein, in an acceptable carrier and administered in 0.5ml intramuscular injectable compositions (see abstract).

The carrier protein was either recombinant Pseudomonas aeruginosa exoprotein A, bovine serum albumin, or formalin-treated exotoxin of C of Clostridium welchii (Pig Bel toxoid) (see page 505, Table 1, and abstract).

(Instant claim 13-17) The composition comprised O157 polysaccharide which was capable of inducing anti-O157 polysaccharide titers (see Table 2, page 5051).
(Instant claim 22 and 24, 26) Anti-O157 specific serum antibody compositions were disclosed (see page 5051, Table 2, col. 2). The reference anticipates the instantly claimed invention.

12. Claims 1-6, 8-11, 13-17, 19-22,24-25, 26, 34-39, 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Konadu et al (symposium and workshop submitted in Applicants USPTO-1449).

Konadu et al disclose the instant claimed invention directed to an O157 O-specific polysaccharide/shiga toxin conjugate (see all slides). Inherently the reference anticipates the instantly claimed invention.

13. Claims 10, 13-18 are rejected under 35 U.S.C. 102(e) as being anticipated by Moreau et al (US Pat. 6,472,506, effective filing date Jan. 21, 1997).
(Instant claim 10, 13-18) Moreau et al disclose the instantly claimed invention directed to a conjugate molecule comprising the E.coli O157:H7 O-specific polysaccharide (see col. 5, line 50, 55-56, lines 35-43) covalently bound to carrier protein (see title), in an acceptable carrier (see col. 7, lines 38-39), together with an adjuvant (see col. 7, line 40) (also see all claims).

14. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Chart et al (J. Clinical Microbiology, 1989).

Chart et al disclose a composition of antibodies immunoreactive with E.coli O157 O-specific polysaccharide (see title, abstract, high titer antibodies IgM against O157; page 287, col. 1, LPS ELISA and col. 2) . Chart et al anticipate the instantly claimed invention.

15. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Vernozy-Rozand, C (May 1997). Vernozy-Rozand, C disclose a composition of antibodies immunoreactive with E.coli O157 O-specific polysaccharide (see page 543, col. 2, paragraph 3, "antisera against O and H antigen", specifically O157") . Vernozy-Rozand, C anticipates the instantly claimed invention.

15. Claims 22-26, 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al (Infection and Immunity, May 1996).

Johnson et al disclose a composition of mammalian serum antibodies immunoreactive with E.coli O157 O-specific polysaccharide and verotoxin (also known as shiga toxin 2, which shares immunoreactivity with Shiga toxin 1) (see title; page 1879, col. 2, paragraph 3; Table 1, page 1880; Table 2, page 1881) . The antibodies were polyclonal antibodies and would be immunoreactive with conserved cross reactive epitopes shared between shiga toxin B-subunit 1 and 2. Johnson et al anticipates the instantly claimed invention.

16. Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by Ashkenazi et al (J. Pediatr. Dec. 1988).

Ashkenazi et al disclose a composition of mammalian serum IVIG antibodies immunoreactive with Shiga toxin and shiga like toxin 1 (see abstract, title, Figure 1, page 1010, Table on page 1012, commercial preparation; Figure 3, page 1012). The antibodies were human polyclonal IgG immunoglobulin fraction antibodies and would be immunoreactive with conserved cross reactive epitopes shared between shiga toxin 1 and 2. Ashkenazi et al anticipates the instantly claimed invention.

17. Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by Britzan et al (1993).

Britzan et al disclose a composition of mammalian plasma (see summary top of page 140, IVIG antibodies immunoreactive with verotoxin (see abstract) which are cross reactive with Shiga toxin (see page 141, col. 1, paragraph 2) Britzan et al anticipates the instantly claimed invention.

18. Claim 40 is rejected under 35 U.S.C. 102(e) as being anticipated by Burnie et al (US Pat. 6,410,024). Burnie et al disclose a composition of serum /antibodies immunoreactive with both Shiga holotoxin (see col. 8, lines 5-17) and E.coli O157:H7 shigalike toxin. Burnie et al anticipates the instantly claimed invention.

19. Claim 22, 24, 26, and 27-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Childlow et al (US Pat. 4,141,970).

Childlow et al disclose antibodies directed against E.coli O157 endotoxin (polysaccharide antigen, see col. 10, claim 6) obtained through active immunization of a pregnant mammal (see all claims, especially claim 6), and also discloses a method of passively immunizing a mammal with anti-O157 antibodies, the method comprising the step of :

administering (see col. 5, lines 18-20) colostrum, IgM and IgG antibodies (see col. 4, lines 22-29) to a mammal, the antibodies comprising a passive immunizing amount of antibody directed against E.coli O157 antigen (see col. 2, lines 32-40, claim 1, claim 6, col. 3, line 11). The antibody dosage was determined based upon titer (see Example 2, col. 5), a high titer of antibody was administered and would be equivalent to the recited 1mg/kg to about 10mg/kg body weight recited in the claims. Childlow et al anticipates the instantly claimed invention.

20. Claims 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Harari et al (June 1988).

Harari et al disclose antibodies specific for Shiga toxin B subunit that are immunoreactive and neutralizing (see title, , page 1619, col. 1, paragraph (ii); Table 2, page 1620; Table 3, page 1622).

Harari et al also disclose a method that comprising administering the anti-shiga toxin antibodies to a mammal in an immunologically effective amount, wherein the mammal was a rat (see page 1620, col. 1, paragraph 2). Harari et al anticipate the instantly claimed invention.

Claim Rejections - 35 U.S.C. § 103

21. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

22. Claims 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robbins et al (1991).

Robbins et al disclose a conjugate molecule that comprises O-specific side chain polysaccharide of Shigella dysenteriae type I, covalently bound to a carrier protein (see page S364, col. 1, paragraph 3), tetanus toxoid, and suggests the B-subunit of Shiga toxin as a carrier protein for the O-specific side chain in light of evidence that serum antitoxin antibodies may reduce the severity of dysentery and diarrhea (see abstract, page S362 and page S364).

It would have been obvious to the person of ordinary skill in the art the time the invention was made of modify the conjugate molecule that comprises O-specific side chain polysaccharide of Shigella dysenteriae type I, covalently bound to a carrier protein (see page S364, col. 1, paragraph 3), tetanus toxoid with the B-subunit of Shiga toxin as a carrier protein for the O-specific side chain as suggested by Robbins et al because Robbins teaches that shiga antitoxin antibodies would provide means for reducing the severity of dysentery and diarrhea associated with shigellosis.

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining and administering a Shigella dysenteria O-specific side chain/ B-subunit of Shiga toxin conjugate to a mammal because the Robbins et al teach a method of obtain the O-specific side chain polysaccharide (see page S363, col. 1, paragraph 3) which serves as a suitable clinical molecule for induction of antibodies to LPS, and the induced antibodies should prevent blood-borne infection (see page S363, col. 1, paragraph 5, last sentence) and confer protection from disease caused by shigellae (see page S363, col. 1, paragraph 1).

In the absence of a showing of unexpected results, Robbins et al obviate the instantly claimed invention.

23. Claims 10-18, 20-21,22, 24,26,27-29, 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konadu et al (1994) in view of Lees (US Pat. 5,693,326).
(Instant claim 10-12, 22) See discussion of Konadu et al above. Konadu et al teach conjugate molecule compositions that comprise E.coli O157:H7 O-specific polysaccharide covalently bound to carrier protein, in an acceptable carrier in an acceptable carrier, but differs from the instantly claimed invention by failing to show the carrier protein to be tetanus toxoid, pertussis toxoid, diphtheria toxoid.

Lees teach the formulation of E.coli O-specific polysaccharide (see col. 11, line 20; col. 30, claim 9; col. 7, lines 50-51) covalently bound to bovine serum albumin, tetanus toxoid, pertussis toxoid or diphtheria toxoid carrier protein, in a dosage form of about 1-20 mg/ml O-specific polysaccharide (carbohydrate, see Lees, col. 9, lines 63-67) and are combined with a carrier (vehicle) and adjuvant (see col. 10, lines 55-68; col. 11, lines 1-5 and line 20) in an analogous art for the purpose of producing immunogenic conjugate molecules for inducing serum antibodies in a mammal (see col. 12, lines 1-5), and for production of antibodies that would serve as diagnostic (see col. 12, lines 6-10) and passive immunotherapeutic agents in a method of passively immunizing a mammal (see col. 12, lines 10-16), wherein the conjugate molecule comprise carbohydrates and proteins the integrity of the structures is maintained, and provides for presentation of native conformation epitopes to a host for induction of an immune response (see col. 4, lines 56-61).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the composition of Konadu et al with the carrier protein of Lees because both Konadu et al and Lees are directed to the production, formulation and utilization of conjugate molecules that comprise a O-specific polysaccharide epitope covalently linked to a carrier protein for administration and induction (see col. 11, lines 61-67) of a protective immune response directed to a mammalian pathogen, wherein the host is a mammal, to include humans (see Lees, col. 11, lines 57-62), and Lees teaches that E.coli O-specific polysaccharides are readily

covalently bound to tetanus toxoid, pertussis toxoid, diphtheria toxoid and the resultant conjugate molecule is immunogenic due to the method of making the conjugate molecules of Lees preserves and maintains the integrity of the polysaccharide and protein structures.

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining conjugate molecules that comprise O-157 O-specific polysaccharide covalently bound tetanus toxoid, pertussis toxoid, or diphtheria toxoid because tetanus toxoid, pertussis toxoid, or diphtheria toxoid have been shown to serve an immunogenic carrier proteins for the induction of an enhanced immune response and also serve to induce an immune response directed against an additional human bacterial pathogen.

24. Claims 4-5, 7, and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Konadu et al (1998) as applied to claims 1-3,6,8-9,10-17,19-26,30-34, 40 above, in view of Lees (US Pat. 5,693,326).

(Instant claim 10-12, 22) See discussion of Konadu et al above. Kondau et al show a conjugate molecule of an O-specific polysaccharide antigen conjugated to the B-subunit of shiga toxin 1 by means of a dicarboxylic acid dihydrazide liner for the purpose of showing conjugate molecules able to induce antibodies directed to both the O-specific polysaccharide antigen and neutralizing antibodies to shiga toxin 1, but differs from the instantly claimed invention by failing to show the utilization of a cyanation process covalently bind the O-specific polysaccharide antigen to the B-subunit of shiga toxin 1

Lees teaches a cyanation process the formulation of conjugate molecules that comprise an E.coli O-specific polysaccharide (see col. 11, line 20; col. 30, claim 9; col. 7, lines 50-51) covalently bound to a carrier protein, and additionally combined with a carrier (vehicle) and adjuvant (see col. 10, lines 55-68; col. 11, lines 1-5 and line 20) in an analogous art for the

purpose of producing conjugate molecules for inducing serum antibodies in a mammal (see col. 12, lines 1-5), and for production of antibodies that would serve as diagnostic (see col. 12, lines 6-10) and passive immunotherapeutic agents in a method of passively immunizing a mammal (see col. 12, lines 10-16), wherein the a cyanation process maintains the integrity of the polysaccharide carbohydrate structures during conjugation of the polysaccharide to the protein carrier (see col. 4, lines 56-61).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the composition of Konadu et al with cyanation means for conjugation as taught by Lees because both Konadu et al and Lees are directed to the production, formulation and utilization of conjugate molecules that comprise a O-specific polysaccharide epitope covalently linked to a carrier protein for administration and induction (see col. 11, lines 61-67) of a protective immune response (see Lees, col. 11, lines 57-62), and Lees teaches a cyanation process which preserves and maintains the integrity of the polysaccharide and protein structures for induction of antibodies which will immunoreact to native epitopes

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining conjugate molecules that comprise O-157 O-specific polysaccharide covalently bound to Shiga toxin B subunit through covalent means through a cyanation process because Lees teaches that through preservation of native epitopes the conjugate molecule serves to induce an enhanced immune response directed against a serious bacterial pathogen.

25. Claim 34-36, 39 is rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (1993) in view of Konadu et al (Feb. 1998).

Taylor et al teach a conjugate molecule that comprises Shigella dyenteriae O-specific polysaccharide antigen conjugated to a carrier protein toxin, but differs from the instantly claimed invention by failing to show the carrier protein toxin to be the B-subunit of shiga toxin 1.

Kondau et al show a conjugate molecule of an O-specific polysaccharide antigen conjugated to the B-subunit of shiga toxin 1 as the carrier protein toxin in an analogous art for the purpose of showing conjugate molecules able to induce antibodies directed to both the O-specific polysaccharide antigen and neutralizing antibodies to shiga toxin 1.

It would have been obvious to the person of ordinary skill in the art the time the invention was made to modify the conjugate molecule of Taylor with the B-subunit shiga toxin protein carrier of Kondau et al because both Taylor and Kondau are directed to the production of O-specific polysaccharide/toxin conjugate molecules and Kondau teaches that the B-subunit of Shiga toxin 1 is able to induce neutralizing antibodies for the complete Shiga toxin 1.

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining neutralizing antibodies directed to two pathogenic specific antigens, because both Taylor and Kondau were able to conjugate the O-PS to the carrier protein while preserving immunogenic pathogen specific epitopes and the conjugate molecule of Kondau was able to induce a very desirable neutralizing antibody directed against Shiga toxin while using the B-subunit of the Shiga toxin as the carrier protein. In the absence of a showing of unexpected results, Taylor in view of Kondau obviate the instantly claimed invention.

Conclusion

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The following references are being made of record and are duplicative to the above applied prior art, but would be applied if necessitated by amendment.

27. Aanon et al (US Pat. 5,204,097); Bundle et al (US Pat. 6,310,043);Chae et al (US Pat. 6,162,441); (Cryz et al (US Pat. 5,370,872); Doyle et al (US Pat. 5,354,661); Keusch et al (5,955,293); Krivan et al (US Pat. 5,512,282); O'Brien et al (US Pat. 5,747,272); Porro (US Pat. 5,153,312); Samuel et al (US Pat. 5,552,144),Dick, WE et al (Contrib. Molecular Immunol. Basel, Karger, 1989, Vol. 10, pages 48-114); Chu et al (Infection and Immunity, 1991); Gupta,

RK et al (Infection and Immunity, 1995); Islam, MS et al (J Clin. Lab. Immunol., 1990); Havens, PL et al (Microb. Immunol. 1992); Padhye, NV et al, (J. Clinic. Microbiol., 1991); Ryd, Marie, PhD thesis, 1992,(Karolinska Institute (Sweden) Vol. 55, 02-C of Dissertation Abstracts International, page 432); Qadri, F et al, (Advances in Mucosal Immunology, 1995); Schmitt et al,(Infection and Immunity, 1991); Weinstein et al (Infection and Immunity, 1989).

28.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242.

The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
July 2, 2003

L. F. S.
LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600